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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,690	12/05/2001	Philip Gerard Cavanaugh		4679

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/002,690	CAVANAUGH, PHILIP GERARD	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *96-115* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *96-115* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 13, 2007 has been entered.

Amendment Entry

2. The amendment filed April 13, 2007 have been entered. The examiner acknowledges the amendments to the specification. Claims 1-96 have been cancelled. Claims 97-115 are newly presented.

Withdrawal of Rejections

3. The following objections and rejections have been withdrawn in view of applicants' amendments:

a) The objection of claim 88;

b) The written description rejection of claims 75-96 under 35 U.S.C. 112, first paragraph;

c) The rejection of claims 75-96 under 35 U.S.C. 112, second paragraph; and

d) The rejection of claims 75-96 under 35 U.S.C. 102(b) as being anticipated by Cavanaugh et al (1998).

Response to Arguments

4. Applicant's arguments with respect to claims 75-96 have been considered but are moot in view of the new ground(s) of rejection.

Claim Objections

5. Claims 97, 109 and 115 are objected to because of the following informalities:

a) Claim 97[b] recites "...allow a binding..." It is suggested that the word "a" be removed. Therefore appropriate correction is required.

b) Claim 109 recites the "said membrane method includes the method of blotting" in the claim. The suggested claim language is "....wherein the applying of said lysate and standards onto the membrane is achieved by a blotting method".

c) Claim 115 states "...is is further comprising..." Appropriate correction is required.

Claim Rejections - 35 USC § 112.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 97-115 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 97 recites "A new method..." The term "new" renders the claim indefinite because it is unclear which limitation is new. Therefore the metes and bounds of the term are unclear. It is suggested that the term be removed.

b) Claim 97[e] recites "applying onto the membrane" however it is unclear what is being applied to the membrane. It is unclear if the lysate is applied to the membrane or if another reagent is applied to the membrane. Therefore it is suggested that the claim recite exactly what is applied to the membrane.

c) Claim 97[f][1] recites "an enzyme-conjugated antibody to said hapten" however it is unclear if the antibody is specific for the hapten. Therefore the suggested claim language is an enzyme-conjugated antibody specific for the hapten-ligand.

d) Claim 97[f][2] recites "a color or light-producing substrate", however the claim does not require that the color or light-producing substrate contact the enzyme in order to produce a signal. Therefore the suggested claim language is a color or light-producing substrate that contacts the enzyme to thereby produce a signal.

e) Claim 99 recites the phrase "is further comprising." The suggested claim language is "further comprises:"

f) Claim 99[a] and [b] recites the limitation "the separating" and "the applying" in the claim. There is insufficient antecedent basis for this limitation in the claim. It is suggested that the word "the" be removed.

g) Claim 100 refers to the Schagger Von Jagow method of electrophoresis. It is unclear what steps and reagents are necessary to perform the method. Therefore the metes and bounds of the electrophoresis are indefinite. Therefore it is suggested that applicant make the article or instructions that disclose the Schagger Von Jagow electrophoresis techniques of record.

h) Claim 101 recites the term "sensitive detecting ...is afforded by the use of said antibodies" in the claim which is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds for determining sensitive detection are unclear. Therefore clarification is required to overcome the rejection.

i) a) Claim 111 recites "a conventional transfer membrane". The term "conventional" renders the claim indefinite because it is unclear what exactly makes the membrane conventional. Thus, the metes and bounds of the term are unclear. It is suggested that the term "conventional" be removed.

Conclusion

8. Claims 97-115 are not rejected under prior art but are rejected under 112 1st and 2nd paragraphs. The closet prior art is Cavanaugh et al., (1998) who teach that transferrin, which is a ligand, binds to a specific cell surface receptor which binds two iron-saturated transferrin molecules and is responsible for the delivery of iron into cells either through internalization of iron-transferrin or activation of a plasma membrane that mediates the trans-plasma membrane transport of iron from transferrin. Cavanaugh et al., teach a process for the evaluation of ligands binding using non-radioisotopic immunologically recognizable hapten-conjugated ligands wherein the conjugated ligands such as rat holo-transferrin purchased from commercial vendors and the fluorescein-conjugated iron saturated (holo) human transferrin obtained from commercial sources. Cavanaugh et al., teach the immunofluorescent detection of the cell surface transferrin, and primary antibody, anti-rat-Transferrin Receptor (TfR), or normal mouse IgG was added to the cells. Cavanaugh et al., teach Fluorescent-activated cell sorting (FACS) analysis was also performed wherein the cells were removed from culture plates; washed; and either normal mouse IgG or anti-rat-TfR was added to the cell and the analyzing the cells by fluorescence using a FACScan instrument. Cavanaugh et al., teach affinity isolation of TfR using immobilized transferrin wherein the transferrin was immobilized on cyanogen bromide activated agarose gel which was later washed to reduce inherent bound transferrin. The lysate supernatant was combined an excess of transferrin agarose and incubated. Lysing steps are equivalent to the claimed solubilization steps. Cavanaugh et al., teach the sample was

separated on a SDS-PAGE gel. Cavanaugh et al., teach the sample was blotted onto commercially available IMMOBILON membrane TM which is a conventional transfer membrane. Cavanaugh et al., teach the membrane was incubated with a commercially available blocking solution containing streptavidin-horseradish peroxidase (HRP). Cavanaugh et al., teach the membrane was washed and the HRP-enhanced chemiluminescence (ECL) substrate which is commercially available was applied and the light-emitting bands were detected and quantitated. Cavanaugh et al., teach an additional procedure based on the affinity isolation of the TfR after biotinylation was used to quantitate cell-surface TfR in the cell lines. Cavanaugh et al., teach the cell surfaces were biotinylated, lysed and the resulting solubilized cell material was exposed to the immobilized transferrin. Cavanaugh et al., teach the agarose-transferrin preferentially bound to biotin-TfR in the lysate which was released with SDS-PAGE separation followed by electrotransfer and detection of biotinylated bands by incubation of the Western blot with streptavidin-HRP followed by ECL.

However Cavanaugh et al., (1998), do not teach or suggest a method for quantifying ligand bind to a surface using hapten-conjugated ligands, comprising:

[a] applying a hapten-ligand, comprising a ligand possessing an antibody-recognizable hapten, onto said surface;

[b] waiting for a period of time, so as to allow a binding of said hapten-ligand to said surface, thereby producing bound ligand;

[c] removing any unbound hapten-ligand, from said surface;

[d] solubilizing said bound ligand, thereby producing a lysate;

[e] applying onto a membrane,

[1] said lysate, and,

[2] standards, comprising solutions containing increasing levels of known amounts of the hapten-ligand, thereby producing membrane-bound hapten-ligand;

[f] applying onto said membrane-bound hapten-ligand,

[1] an enzyme-conjugated antibody to said hapten, and

[2] a color or light-producing substrate for said enzyme, thereby producing a signal; [g] comparing said signal arising from said enzyme associated with said membrane-bound hapten-ligand arising from said standards, to the known amount of hapten-ligand contained in said standards, thereby producing a standard curve;

[h] comparing said signal arising from said enzyme associated with said membrane-bound hapten-ligand arising from said lysate, to said standard curve, thereby quantifying the amount of the hapten-ligand contained in said membrane-bound hapten-ligand arising from said lysate, whereby the quantifying of the amount of the membrane-bound hapten-ligand arising from said lysate, is used to quantify the amount amount of said hapten-ligand originally bound to said surface, and, whereby the use of radio-labeled ligand is avoided.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Jeffery Siew, can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
June 22, 2007

MARK NAVARRO
PRIMARY EXAMINER